

CAUSE NO. 2001-61352

BAYLOR COLLEGE OF MEDICINE (IN THE DISTRICT COURT OF
and BCM TECHNOLOGIES, INC. (

(
Vs. (HARRIS COUNTY, T E X A S
CLONTECH LABORATORIES, INC. (

(
VS. (

(
INVITROGEN CORPORATION (133RD JUDICIAL DISTRICT

ORAL DEPOSITION OF
STEPHEN ELLEDGE, Ph.D.
MARCH 26, 2003

Reported by: LINDA RAYBURN
Job No. 40456



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EXHIBIT INDEX

10 Number

Description

Page Marked

11 30 Expert Report of Stephen
Elledge, Ph.D.

7

13 31 E-mail string with production
Numbers BCM 003154-55

43

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ORAL DEPOSITION OF STEPHEN ELLEDGE, Ph.D.

1 ORAL DEPOSITION OF STEPHEN ELLEDGE Ph.D., produced as
2 a witness at the instance of the DEFENDANT/COUNTERCLAIM
3 PLAINTIFF, and duly sworn, was taken in the above-styled
4 and numbered cause on MARCH 26, 2003, from 9:04 a.m. to
5 11:20 a.m., before Linda Rayburn, CSR in and for the
6 State of Texas, reported at Baylor College of Medicine,
7 1 Baylor Plaza, Cullen Building, Suite 106-A, Houston,
8 Texas, pursuant to the Texas Rules of Civil Procedure
9 and the provisions stated in the record or attached
10 hereto.

11

12

A P P E A R A N C E S

13

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16 MS. MICHELLE MULLER
17 Vinson & Elkins
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-AND-

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23 FOR THE DEFENDANTS/COUNTERCLAIM PLAINTIFF:

24 MR. MARC R. LABGOLD
25 Patton Boggs, LLP
8484 Westpark Drive, Suite 900

ORAL DEPOSITION OF STEPHEN ELLEDGE, Ph.D.

1 of the Univector system.

2 Q , And in fact, all of the elements of the
3 Univector system, and take it in unconnected form, were
4 all known in the prior art, correct?

5 A It depends on what you mean by "elements." I
6 don't know what you mean, so perhaps you could define
7 that for me, because it's a very vague term.

8 Q Why don't you tell me what makes up the
9 Univector system.

10 MR. BLANKE: Objection, form.

11 Q (By Mr. Labgold) Or why don't you -- I'll make
12 it a little more defined. What do you consider to be
13 the essential elements of the Univector system?

14 MR. BLANKE: Objection, form.

15 THE WITNESS: I consider the essential
16 elements of the Univector system to be the ability to
17 cause the fusion between two molecules using
18 site-specific recombination, one of those molecules
19 being a recipient vector, the other being a donor vector
20 that contains site-specific recombination site, a drug
21 marker and the absence of a functional origin under
22 certain conditions --

23 Q And --

24 A The ability to select for that event.

25 Q Now, the prior art taught site-specific

ORAL DEPOSITION OF STEPHEN ELLEDGE, Ph.D.

1 recombination, correct?

2 A That is correct.

3 Q And the prior art taught the use of lox sites
4 for site-specific recombination, correct?

5 A That is correct.

6 Q And the prior art taught Cre-mediated
7 recombination using the lox sites?

8 A That is correct.

9 Q And the prior art taught drug resistance
10 markers, right?

11 A Correct.

12 Q And the prior art taught conditional origins of
13 replication, correct?

14 A Correct.

15 Q And the prior art, one that you didn't mention
16 here, but I think is also important to the system,
17 correct me if I'm wrong, the prior art taught cells
18 which would allow for the selection of the conditional
19 origin of replication, correct?

20 A That is correct.

21 Q So --

22 A And also, I would add, I don't know, "element"
23 is a -- I mean, there is also the concept of the purpose
24 of making the fusion event to create expression vectors
25 and things like that. That was a novel element.

ORAL DEPOSITION OF STEPHEN ELLEDGE, Ph.D.

1 Q Well, expression vectors were known before,
2 correct?

3 A Right. But I think the use of site-specific
4 recombination in this way wasn't appreciated, so that
5 that I think is a novel element, because without the
6 need to do that, there would be no coming together of
7 the other elements.

8 Q But prior to your invention, people clearly
9 desired and actually accomplished the ability to
10 subclone pieces of DNA from one vector to another,
11 correct?

12 A Yes, using conventional methods.

13 Q And some of those conventional methods would be
14 what I would refer to as kind of traditional subcloning
15 where you excise a DNA sequence of interest from one
16 plasmid using restriction enzymes and put them into
17 another plasmid having complementary restriction sites,
18 correct?

19 A That's correct.

20 Q And in certain circumstances, the first vector
21 would be what might be called a cloning vector which was
22 unable to express the gene of interest, correct?

23 A Yes, that's one example.

24 Q And one of the purposes for wanting to subclone
25 this gene of interest from that cloning vector is to put

ORAL DEPOSITION OF STEPHEN ELLEDGE, Ph.D.

1 it into what we call an expression vector so that the
2 gene of interest would be juxtaposed in proper reading
3 frame with a promoter, correct?

4 A That is correct.

5 Q And therefore that would allow for the
6 expression in the host cell under the right conditions
7 of the gene of interest, correct?

8 A Yes.

9 Q And so is it fair to say that the -- do you
10 understand the word "novelty" as it --

11 A I have an understanding of it, yes.

12 Q Okay. Well, for the sake of getting past the
13 point, would it be fair to say that the novelty of your
14 system was not that it had new elements, but that these
15 elements were arranged in a way that had not been
16 previously arranged to achieve the result which you
17 achieved?

18 A Yes.

19 Q Now, you filed a patent application on which
20 you consider to be your invention, correct?

21 A That is correct.

22 MR. LABGOLD: And I apologize. I did not,
23 as I was handing out all those extra copies, one of the
24 reasons was I was supposed to have an extra copy for
25 today. Do you have yesterday's exhibits?

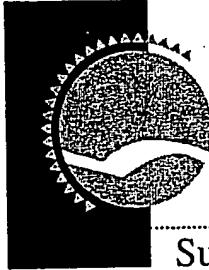
CAUSE NO. 2001-61352

Baylor College of Medicine (IN THE DISTRICT COURT OF
and BCM TECHNOLOGIES, INC. ()
Vs. ()
CLONTECH LABORATORIES, INC. (HARRIS COUNTY, T. E X A S
VS. ()
INVITROGEN CORPORATION (133RD JUDICIAL DISTRICT

ORAL DEPOSITION OF
KENNETH N. KREUZER, Ph.D.
MARCH 25, 2003

Reported by: LINDA RAYBURN
Job No. 40429

**EXHIBITS
BOUND
SEPARATELY**



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13 2	Article, "Escherichia coli genome	
14	targeting"	75
15 3	Collection of 44 figures from	
16	U.S. Patent 5,888,732	95
17 4	U.S. Patent Number 5,888,732U	96
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ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.,
2 produced as a witness at the instance of the
3 DEFENDANT/COUNTERCLAIM PLAINTIFF, and duly sworn, was
4 taken in the above-styled and numbered cause on MARCH
5 25, 2003, from 10:00 a.m. to 2:22 p.m., before Linda
6 Rayburn, CSR in and for the State of Texas, reported at
7 the offices of Vinson & Elkins, 1001 Fannin Street,
8 Suite 2300, Houston, Texas, pursuant to the Texas Rules
9 of Civil Procedure and the provisions stated in the
10 record or attached hereto.

11

12 A P P E A R A N C E S

13

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23

24

* * * * *

25

ORAL DEPOSITION OF KENNETH N. KRUEZER, Ph.D.

1 to "donor vector," which we see down a little further on
2 the page?

3 A Sure.

4 Q And one last question and we'll take our break.
5 Your definition of "donor vector," is that concept there
6 something which was invented by Dr. Stephen Elledge?

7 A I think it would be the same answer as before.

8 MR. LABGOLD: Why don't we go ahead and
9 take a quick break.

10 (A recess was taken.)

11 Q (By Mr. Labgold) Back to our Glossary of
12 Terms, I assume you will agree with me that Dr. Elledge
13 did not invent the concept of antibiotics?

14 A Certainly.

15 Q And you also agree that he did not invent the
16 idea of using antibiotic resistant genes as selection
17 markers?

18 A Yes.

19 Q Conditional origin of replication, is that a
20 concept which was invented by Dr. Elledge?

21 A No.

22 Q Do you know if it was published in the art
23 before the development of the Univector system?

24 A Sure.

25 Q And do you know if its use in cloning

ORAL DEPOSITION OF KENNETH N. KR^OZER, Ph.D.

1 technologies was discussed in the literature prior to
2 the Elledge Univector development?

3 A Yes.

4 Q Are you aware -- pardon me?

5 A It's used in a variety of situations.

6 Q Are you aware that Dr. Elledge received certain
7 bacterial strains from a Dr. Barry Wanner at Purdue?

8 A Yes.

9 Q And are you aware of the fact that Dr. Elledge
10 provided those strains to Clontech without advising
11 Dr. Wanner of that fact beforehand?

12 MR. BLANKE: Objection, form.

13 THE WITNESS: I don't know what the
14 communication was between Dr. Elledge and Dr. Wanner.

15 Q (By Mr. Labgold) Have you seen that allegation
16 in the record?

17 A The allegation that it was provided without
18 proper communication?

19 Q Yes.

20 A I think I have, yes.

21 Q Have you seen -- I believe in your report you
22 indicated that you've seen all of the documents that
23 have been produced by both parties; is that correct?

24 A As far as I know. I came to Austin and was
25 presented with what was thirteen or fifteen boxes of

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 with licensing.

2 Q That there was a third-party that had certain
3 rights to the GST fusion purification system? That's
4 what the concern was?

5 A That's my recollection.

6 Q And from your review of the documents, Clontech
7 was cognizant of the fact that they did not want to use
8 someone else's technology?

9 A Hang on a minute. I could be wrong, but that's
10 my recollection at the moment.

11 Q And Dr. Elledge did not invent GST fusion
12 proteins, correct?

13 A No.

14 Q That's correct or not correct?

15 A Oh, sorry. Dr. Elledge did not invent GST
16 fusion proteins as a general entity, yes.

17 Q And he did not invent the concept of creating a
18 GST fusion so that the protein to which the GST was
19 fused could be purified, correct?

20 A That's correct.

21 Q And in fact, the publication, itself, makes
22 reference to that and being in the prior art, correct?

23 A Yes.

24 Q Did you review the correspondence between
25 Clontech and Dr. Elledge concern Clontech's efforts to

ORAL DEPOSITION OF KENNETH N. KREUZER, PH.D.

(Discussion off the record.)

2 Q / (By Mr. Labgold) I would like to mark as
3 Kreuzer Exhibit 3 a publication in Gene, the journal
4 Gene, G-e-n-e, Volume 150, 1994, Pages 51 to 56,
5 entitled, "Escherichia coli genome targeting, I.
6 Cre-lox-mediated in vitro generation of ori minus
7 plasmids and their in vivo chromosomal integration and
8 retrieval."

11 MR. LABGOLD: Back on the record here. We
12 have misidentified it. This article, Hasan, et al.,
13 from Dr. Szybalski's lab will be Exhibit 2.

14 Q (By Mr. Labgold) If you'd take a moment to
15 look at this article and tell me if you've seen this
16 before?

17 A I believe I've seen a related paper. It may
18 be -- maybe it's number two in the series. I'm not sure
19 I've seen this one.

20 Q And do you understand this as being -- where it
21 says Cre-lox-mediated, this is the same type of Cre-lox
22 recombination that we're talking about, correct?

23 A That would be -- the reaction, itself, would be
24 the same kind of reaction, yes.

25 Q And do you understand that this is a -- a

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 method for inserting genes of interest into an acceptor
2 molecule, in this case a chromosome?

3 A Again, I would need some time to read through
4 the paper carefully, but it seems -- seems like that's
5 what the title and abstract are, just guessing.

6 Q And to the extent you need to review any of it
7 in detail, please take as much time as you need. Would
8 you agree that the article describes putting a gene of
9 interest onto a -- a plasmid -- well, let's take a look
10 at Figure 1.

11 A Okay.

12 Q And why don't you take a moment to read the
13 legend to Figure 1.

14 A Okay.

15 Q And do you have a general understanding of
16 what's represented by this figure?

17 A Yes, I think so.

18 Q And is it your understanding that the top
19 plasmid, the top circle there, pNH64a, is used to -- as
20 a vector for a gene of interest?

21 A Yes.

22 Q And that that vector contains the two loxP
23 sites?

24 A Yes.

25 Q Which when subjected to the Cre enzyme in vitro

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 results in a recombination event that yields two
2 plasmids that are shown as pNH64b and pNH64c?

3 A Yes.

4 Q Now, what's your understanding of that ori
5 minus notation?

6 A That's a circular fragment of DNA that will go
7 on to insert into bacterial chromosome.

8 Q And by it being ori minus, that means that that
9 plasmid cannot propagate in a host organism, correct?

10 A At least not a wild type host organism.

11 Q And that ori minus feature is used as a
12 selection for the desired reaction, correct?

13 A Yes, it's used as a negative selection for the
14 desired reaction. Not the reaction that's shown here.

15 Q Correct.

16 A The reaction that occurs later.

17 Q And if I understand what is intended to happen
18 next is that the result of the in vitro recombination
19 with Cre -- oh, and let me ask you this, backing up a
20 step. You've described in your expert report that this
21 Cre-mediated reaction is a reversible reaction, correct?

22 A Yes.

23 Q So that where it shows an arrow coming from the
24 big plasmid on the top of Figure 1 of Kreuzer Exhibit 2,
25 down to the two daughter plasmids, that's actually -- it

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 should be a two-way arrow, correct?

2 A Yes.

3 Q And that I believe -- and I apologize, because
4 I don't know exactly where the citation is in your --
5 oh, I believe if you go to Page 21, I'm sorry, you state
6 that after the two -- do you see about halfway down
7 Page 45?

8 A Yes.

9 Q "After the two have been mixed together in the
10 presence of Cre, you will have a mixture of vectors.
11 Because the Cre reaction is reversible, vectors will be
12 fusing and separating in the test tube until you stop
13 the reaction."

14 A Yes.

15 Q And so that type of reversible equilibrium is
16 actually going on in this reaction, too, correct?

17 A Yes, I mean, as I indicated in the report,
18 depending on the DNA concentration, you can push it one
19 way or the other.

20 Q And what's not shown in Figure 1 of Kreuzer
21 Exhibit 2 is that you then transform this into a host
22 organism, correct?

23 A Correct.

24 Q And then the chromosome of that host organism
25 works as an acceptor molecule, if you will, for

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 Q And by that system, you have a selection
2 mechanism so that you can select for a resulting
3 organism that displays the gene of interest and you will
4 know by the means of the selection that you've got the
5 right mutagenized product, correct?

6 A You would certainly want to confirm it, but you
7 would -- if the system works properly, you would have
8 that, yes. And again, I haven't looked past Figure 1,
9 so I'm assuming the system works by the lambda
10 recombination. Right. And that's clearly indicated in
11 the abstract.

12 Q Uh-huh. Now, if Dr. Elledge was aware of this
13 paper before the development of the Univector system,
14 would the ethic provide that he should cite this
15 reference in his article?

16 A I don't particularly see why at the moment. I
17 don't think his system is built on this at all.

18 Q Even though it uses several of the key elements
19 here?

20 A As you pointed out before, there were quite a
21 number of papers that use lox-mediated recombination in
22 a variety of situations.

23 Q And this one actually goes through taking a
24 gene of interest, putting it into a plasmid, creating a,
25 you know, donor plasmid, if you will, in the ori minus?

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 A The words "donor" and "acceptor" don't mean
2 very much. The heart of the Elledge system, you know,
3 as I indicated, is the ability to make novel gene
4 combinations, gene fusions, promoter gene constructs.
5 And, you know, other people, as I said before, have used
6 lox sites, for example, to introduce mutations into
7 mouse gene targeting. Those are interesting other
8 applications of lox recombination, but I don't think
9 that the Elledge system is built on any of those, you
10 know, as far as I can see.

11 Q Uh-huh. Would you agree that the insertion of
12 the gene of interest, the recombination event in Kreuzer
13 Exhibit 2 into the chromosome is also a reversible
14 reaction?

15 A I don't believe that it is in the cells that
16 they use. Int is -- only refers to when another protein
17 is present, and I doubt if they have that protein
18 present in the cells. But I would have to look at the
19 materials and methods to determine that.

20 Q And what's the enzyme, the protein that you are
21 referring to?

22 A XIS, X-I-S. I would -- again, I would have to
23 look over it carefully. The normal -- let me clarify.
24 The normal lambda integration which uses -- in the case
25 of the Int protein, the two sites are different, they

ORAL DEPOSITION OF KENNETH N. KREUZER, Ph.D.

1 are not the same as with the Cre-lox system. And the
2 normal reaction which occurs between the two different
3 sites goes in one direction with Ints and requires an
4 XIS for the reverse direction.

5 I would have to look over this more
6 carefully to see. It looks to me like they are using
7 the normal bacterial -- they are using the normal
8 combination of two sites, and so my presumption, if that
9 is true, is that it would require a second protein.

10 Q If you'd take a look at Page 55, Subsection D.

11 A Okay.

12 Q And take as much time as you need to read that
13 section and just --

14 MR. BLANKE: We're on Exhibit 2 of the
15 Kreuzer deposition?

16 MR. LABGOLD: Yes, sir. I'm sorry,
17 Kreuzer Exhibit 2 at Page 55. And it's in bold,
18 Subsection D on the left-hand column.

19 THE WITNESS: Okay. Yes.

20 Q (By Mr. Labgold) Doesn't this indicate that
21 the inserted gene product can actually be retrieved from
22 the chromosome?

23 A By introducing the excising protein.

24 Q Now, if you go to Page 22 of your report, which
25 is Kreuzer Exhibit 1, at the top of the page, you have a

Mr. Richard J. Oparil

Page 4

May 2, 2003

c: Glenn A. Ballard, Jr. (*by fax*)
Tracey B. Davies [Firm]
M. Michelle Muller [Firm]
Jason M. Powers [Firm]

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3 MAY -2 P6:29

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FACSIMILE TRANSMITTAL PAGE

DATE: May 2, 2003

TO: Glenn A. Ballard, Jr.
Bracewell & Patterson

FAX: 713.221.1212

PHONE: 713.223.2900

TO: Richard J. Oparil
Patton Boggs (DC)

FAX: 202.457.6315

PHONE: 202.457.6000

PAGES: 5 (including this transmittal page)

CLIENT/MATTER: INV850/13000

FROM: David P. Blanke

MESSAGE: David Blanke's 05/02/03 letter to Oparil re agreements to narrow issues in Clontech's motion to compel discovery from Baylor.

Hard Copy Follows: Yes No

CONFIDENTIALITY NOTICE:

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May 6, 2003

By Fax

Mr. Richard J. Oparil
Patton Boggs L.L.P.
2550 M Street NW
Washington, DC 20037

Re: *Baylor College of Medicine, et al. v. Clontech Laboratories, Inc.*:
Cause No. 2001-61352

Dear Richard:

I am further responding to your April 14 letter. Earlier I wrote regarding the Ruobo Zhang exhibits. As to the '808 continuations, we will be producing the non-privileged documents on this issue. In the meantime, I am providing the accompanying preliminary amendment and notice of allowance from the PTO.

Very truly yours,



David P. Blanke

attachment

c: Glenn A. Ballard, Jr. (by fax; w/att.)
Kevin Bell (by fax; w/att.)
Tracey B. Davies [Firm; w/o att.]
M. Michelle Muller [Firm; w/o att.]
Jason M. Powers [Firm; w/o att.]



UNITED STATES DEPARTMENT OF COMMERCE

Patent and Trademark Office

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Washington, D.C. 20231

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR/ PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT PAPER

47

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

-See attached--

Notice of Allowability

Application No.

09/122,384

Applicant(s)

ELLEDGE ET AL.

Examiner

Art Unit

James S. Ketter

1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--
 Claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included
 herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. THIS
NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative
 of the Office or upon petition by the applicant. See 37 CFR 1.513 and MPEP 1308.

- This communication is responsive to the amendment of 10/3/02 and the IDS of 3/4/03.
- The allowed claim(s) is/are 43-58.
- The drawings filed on 20 March 2001 are accepted by the Examiner.
- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some c) None of the:
1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____.
- Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- (a) The translation of the foreign language provisional application has been received.
- Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF FORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

CORRECTED DRAWINGS must be submitted.

(a) including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 1) hereto or 2) to Paper No. _____.

(b) including changes required by the proposed drawing correction filed _____ which has been approved by the Examiner.

(c) including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- Notice of References Cited (PTO-892)
 Notice of Draftsperson's Patent Drawing Review (PTO-948)
 Information Disclosure Statements (PTO-1449), Paper No. 70 42 4r.
 Examiners Comment Regarding Requirement for Deposit
 of Biological Material

- Notice of Informal Patent Application (PTO-152)
 Interview Summary (PTO-413), Paper No. _____.
 Examiner's Amendment/Comment
 Examiner's Statement of Reasons for Allowance
 Other


 JAMES KETTER
 PRIMARY EXAMINER



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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176

NOTICE OF ALLOWANCE AND FEE(S) DUE

21586 7500 04/22/2003

VINSON & ELKINS, L.L.P.
1001 FANNIN STREET
2300 FIRST CITY TOWER
HOUSTON, TX 77002-6760

RECEIVED

APR 28 2003

IP Docket Office
Vinson & Elkins

EXAMINER

KETTER, JAMES S

ART UNIT

CLASS-SUBCLASS

1036

435-006000

DATE MAILED: 04/22/2003

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN A. ELEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1300	\$0	\$1300	07/22/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED, SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-8SB (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

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If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

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B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

Applicant claims SMALL ENTITY status.
See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

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Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE

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31586 7590 04/22/2003

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1001 FANNIN STREET
2300 FIRST CITY TOWER
HOUSTON, TX 77002-6760

NOTE: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,184	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION.

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1300	\$0	\$1300	07/22/2003

EXAMINER	ART UNIT	CLASS-SUBCLASS
KETTER, JAMES S	1636	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

"Fee Address" indication (or "Fee Address" indication form PTO/SB/47; Rev 01-02 or more recent) attached. Use of a Customer Number is required.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) individual corporation or other private group entity government

4a. The following fee(s) are enclosed:

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Issue Fee
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 Advance Order - # of Copies _____

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Payment by credit card. Form PTO-2038 is attached.

The Commissioner is hereby authorized to charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLIDGE	BAY 136/4-010CIP	6340
21586	7590	04/22/2003	EXAMINER	
VINSON & ELKINS, L.L.P. 1001 FANNIN STREET 2300 FIRST CITY TOWER HOUSTON, TX 77002-6760			KETTER, JAMES S	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 04/22/2003				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
 (application filed on or after May 29, 2000)

The patent term adjustment to date is 0 days. If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the term adjustment will be 0 days.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (<http://pair.uspto.gov>)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010CIP	4340
21586	7590	04/22/2003	EXAMINER	
VINSON & ELKINS, L.L.P. 1001 FANNIN STREET 2300 FIRST CITY TOWER HOUSTON, TX 77002-6760 UNITED STATES			KETTER, JAMES S	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 04/22/2003				

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003: Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: <http://www.uspto.gov/main/howfees.htm>.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Vinson & Elkins
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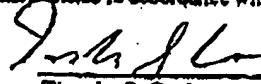
Timothy S. Corder
Direct Dial 512-542-8446
Direct Fax 512-236-3377
tcorder@velaw.com

October 3, 2002

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002
Date


Timothy S. Corder

Assistant Commissioner for Patents
Washington, D.C. 20231

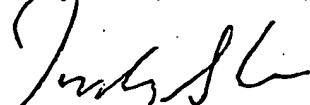
Re: U.S. Patent Application SN 09/122,384 "Rapid Subcloning Using Site-Specific Recombination," by Elledge et al.
Attorney Docket No.: BAY136/4-010CIP/36000; Client Ref.: OTA # 97-27
Confirmation No. 4340

Sir:

Enclosed for filing in the above-referenced patent application is a Preliminary Amendment for filing in the above-referenced patent application.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to appropriately deduct or credit the requisite amount from Vinson & Elkins L.L.P. deposit account No. 22-0365/BAY136/4-010CIP/36000.

Respectfully submitted,


Timothy S. Corder
Reg. No. 38,414

9282:5588

Enclosure

311728_1.DOC

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Stephen J. Elledge et al.

Serial No.: 09/122,384

Filed: July 24, 1998

For: Rapid Subcloning Using Site-Specific Recombination

Group Art Unit: 1636

Examiner: J. Ketter

Art. Dkt. No.: BAY136/4-10CIP/36000

Confirmation No. 4340

CERTIFICATE OF FACSIMILE

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October 3, 2002


Timothy S. Corder

PRELIMINARY AMENDMENT

VIA FACSIMILE NO. 703-746-5155

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, the Examiner is requested to please amend the above-captioned application as follows:

AMENDMENT

A. In the Claims:

Please cancel all pending claims, i.e. claims 1-20, 26, 30-35, and 37-42, and enter the following new claims:

43. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

44. The composition of claim 43, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.
45. The composition of claim 43, wherein the composition comprises an enzyme activity with a Cre recombinase efficiency of about 16.8% per microgram of protein.
46. An isolated nucleic acid molecule comprising a coding region wherein the coding region encodes a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
47. The nucleic acid molecule of claim 46, wherein the coding region comprises the nucleic acid sequence of SEQ ID NO:10.
48. The nucleic acid molecule of claim 46, wherein the isolated nucleic acid molecule is an expression vector.
49. The nucleic acid molecule of claim 46, wherein the coding region is operatively linked to a promoter effective to direct expression of a glutathione-S-transferase-Cre recombinase fusion polypeptide.
50. The nucleic acid molecule of claim 49, wherein the promoter is an inducible promoter.
51. The nucleic acid of claim 50, wherein the promoter is the *lac* promoter.
52. A host cell comprising the nucleic acid molecule of claim 46.
53. A host cell comprising the nucleic acid molecule of claim 49.
54. The host cell of claim 53, wherein the host cell expresses a Cre recombinase activity.

- () ()
55. The host cell of claim 53, further defined as an E. coli cell.
56. A bacterial cell engineered to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
57. The bacterial cell of claim 56, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.
58. A method of producing a glutathione-S-transferase-Cre-recombinase fusion polypeptide comprising:
obtaining an expression vector comprising a coding region encoding a glutathione-S-transferase-Cre-recombinase fusion polypeptide operatively linked to a promoter;
transforming or transfecting the vector into a cell; and
growing the cell under conditions effective to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
59. The method of claim 58, further comprising isolating the glutathione-S-transferase-Cre-recombinase fusion polypeptide.
60. The method of claim 59, wherein isolating the polypeptide comprises glutathione affinity chromatography.
61. A method of recombining nucleic acid segments, wherein each segment comprises a *lox* site specific recombinase site, the method comprising contacting the nucleic acid segments with a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
62. The method of claim 61, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

63. A composition comprising a glutathione-S-transferase-Cre recombinase fusion polypeptide and one or more nucleic acid molecules, wherein the nucleic acids comprise a site specific recombinase site.
64. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a lox recombination site upstream in a 5' to 3' orientation from an amino acid encoding region.
65. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a transcription regulatory element upstream in a 5' to 3' orientation of a lox recombinase site.
66. The composition of claim 64 wherein the lox recombinase site is a *loxP*, *loxP2*, *loxP3*, *loxP23*, *loxP511*, *loxB*, *loxC2*, *loxL*, *loxR*, *lox186*, *lox117*, or *loxH* site.
67. The composition of claim 65 wherein the lox recombinase site is a *loxP*, *loxP2*, *loxP3*, *loxP23*, *loxP511*, *loxB*, *loxC2*, *loxL*, *loxR*, *lox186*, *lox117*, or *loxH* site.
68. The composition of claim 64, wherein the amino acid encoding region is a member of a nucleic acid library.

II. REMARKS

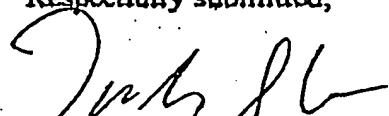
The claims in this preliminary amendment do not add new matter to the application and their entry is therefore respectfully requested. Support for the claims may be found throughout the Specification and at least in Example 3 found on page 47.

IV. CONCLUSION

Applicants respectfully submit that the present application and all claims are in condition for immediate allowance and early notice to such effect is earnestly solicited. If, in the opinion of the Examiner, a phone call may help expedite prosecution of this application, the Examiner is invited to contact the undersigned representative at (512) 542-8446.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Vinson & Elkins L.L.P. Deposit Account No. 22-0365/BAY136/4-10CIP/36000.

Respectfully submitted,



Timothy S. Corder
Reg. No. 38,414
Agent for Applicant

Vinson & Elkins L.L.P.
2300 First City Tower
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Houston, Texas 77002-6760
512/542-8446

Date: October 3, 2002

Vinson & Elkins
ATTORNEYS AT LAW

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5 MAY -6 P1:59

David P. Blanke
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Direct Fax (512) 236-3314
dblanke@vclaw.com

FACSIMILE TRANSMITTAL PAGE

DATE: May 6, 2003

Glenn A. Ballard, Jr.
Bracewell & Patterson

FAX: 713.221.1212

PHONE: 713.223.2900

TO: Marc Labgold
Kevin M. Bell
Patton Boggs (VA)

FAX: 703.744.8001

PHONE: 703.744.8000

TO: Richard J. Oparil
Patton Boggs (DC)

FAX: 202.457.6315

PHONE: 202.457.6000

PAGES: 14 (including this transmittal page)

CLIENT/MATTER: INV850/13000

FROM: David P. Blanke

MESSAGE: David Blanke's 05/06/03 letter further responding to 04/14/03 Oparil letter.

Hard Copy Follows: Yes No

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PATTON BOGGS LLP
ATTORNEYS AT LAW

2550 M Street NW
Washington DC 20037
(202) 457-6000

Facsimile (202) 457-6315

To: **Amy Bell**
Company: **Patton Boggs LLP**
Fax Number: **703.744.8001**
Phone Number: **703.744.8000**

Total Pages
Including Cover: **15**

From: **Richard Oparil**
Sender's Direct Line: **202.457.6496**
Date: **May 6, 2003**
Client Number: **020187.0102**

Comments:

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5 MAY -6 P1:59

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FACSIMILE TRANSMITTAL PAGE

DATE: May 6, 2003

Glenn A. Ballard, Jr.
Bracewell & Patterson

FAX: 713.221.1212

PHONE: 713.223.2900

TO: Marc Labgold
Kevin M. Bell
Paton Boggs (VA)

FAX: 703.744.8001

PHONE: 703.744.8000

TO: Richard J. Oparil
Paton Boggs (DC)

FAX: 202.457.6315

PHONE: 202.457.6000

PAGES: 14 (including this transmittal page)

CLIENT/MATTER: INV&50/13000

FROM: David P. Blanke

MESSAGE: David Blanke's 05/06/03 letter further responding to 04/14/03 Oparil letter.

Hard Copy Follows Yes No

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MAY 06 2003 12:50 PM FR VINSON & ELKINS 512 542 8612 TO 8895302#91202457 P.02/14

Vinson & Elkins
ATTORNEYS AT LAW

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May 6, 2003

By Fax

Mr. Richard J. Oparil
Parton Boggs L.L.P.
2550 M Street NW
Washington, DC 20037

Re: *Baylor College of Medicine, et al. v. Clontech Laboratories, Inc.*:
Cause No. 2001-61352

Dear Richard:

I am further responding to your April 14 letter. Earlier I wrote regarding the Ruobo Zhang exhibits. As to the '808 continuations, we will be producing the non-privileged documents on this issue. In the meantime, I am providing the accompanying preliminary amendment and notice of allowance from the PTO.

Very truly yours,



David P. Blanke

attachment

- c: Glenn A. Ballard, Jr. (by fax; w/att.)
Kevin Bell (by fax; w/att.)
Tracey B. Davies [Firm; w/o att.]
M. Michelle Muller [Firm; w/o att.]
Jason M. Powers [Firm; w/o att.]



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Patent and Trademark Office

Address: ASSISTANT COMMISSIONER FOR PATENTS

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APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.

EXAMINER

ART UNIT PAPER

47

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

--See attached--

Notice of Allowability

Application No.	Applicant(s)
09/122,384	ELLEDGE ET AL.
Examiner	An Unit
James S. Ketter	1836

- The MAILING DATE of this communication appears on the cover sheet with the correspondence address-

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS. This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.913 and MPEP 1308.

1. This communication is responsive to the amendment of 10/3/02 and the IDS of 3/4/03.

2. The allowed claim(s) is/are 43-68.

3. The drawings filed on 20 March 2001 are accepted by the Examiner.

4. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some* c) None of the:

1. Certified copies of the priority documents have been received.

2. Certified copies of the priority documents have been received in Application No. _____.

3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

5. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

(a) The translation of the foreign language provisional application has been received.

6. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

7. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. CORRECTED DRAWINGS must be submitted.

(a) including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
1) hereto or 2) to Paper No. _____.

(b) including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.

(c) including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|---|--|
| <input type="checkbox"/> Notice of References Cited (PTO-892) | <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | <input type="checkbox"/> Interview Summary (PTO-413), Paper No. _____ |
| <input checked="" type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. 70 12 § yr. | <input type="checkbox"/> Examiner's Amendment/Comment |
| <input type="checkbox"/> Examiners Comment Regarding Requirement for Deposit of Biological Material | <input type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | <input type="checkbox"/> Other |



JAMES KETTER
PRIMARY EXAMINER



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES PATENT AND TRADEMARK OFFICE
United States Patent and Trademark Office
Aeronautics and Space
Washington, D.C. 20231
www.uspto.gov

NOTICE OF ALLOWANCE AND FEE(S) DUE

21386 7300 04/22/2003

VINSON & ELKINS, L.L.P.
1001 FANNIN STREET
2300 FIRST CITY TOWER
HOUSTON, TX 77002-6760

RECEIVED

APR 28 2003

IP Docket Office
Vinson & Elkins

EXAMINER	
KETTER, JAMES S	
ART UNIT	CLASS-SUBCLASS
1636	615-006000
DATE MAILED: 04/22/2003	

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN L. ELLEDGE	BAY1364-010CIP	4340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1300	\$0	\$1300	07/22/2003

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-SSB (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

Applicant claims SMALL ENTITY status.
See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Box ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail Box ISSUE FEE

Commissioner for Patents
Washington, D.C. 20231
FAX (703)746-4000

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for transmission by facsimile.

CONFIRMATION CORRESPONDENCE ADDRESS (Please supply name and address of law firm if any)

31346 7390 04/22/2003

VINSON & ELKINS, L.L.P.
1001 FANNIN STREET
2300 FIRST CITY TOWER
HOUSTON, TX 77002-5760

Note: A certificate of mailing can only be used for domestic filings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission
I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Box Issue Fee address above, or being facsimile transmitted to the USPTO on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/122,384	07/24/1998	STEPHEN J. ELEDGE	BAY1364-Q10CIP	6340

TITLE OF INVENTION: RAPID SUBCLONING USING SITE-SPECIFIC RECOMBINATION.

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
PROVISIONAL	NO	\$1300	\$0	\$1300	07/22/2003

EXAMINER	ART UNIT	CLASS-SUBCLASS
KETTER, JAMES S	1636	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.563).

Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

"Fee Address" indication (or "Fee Address" indication form PTO/SB/47; Rev 03-02 or more recent) attached. Use of a Customer Number is required.

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) Individual corporation or other private group entity government

4a. The following fee(s) are enclosed:

4b. Payment of Fee(s):

Issue Fee

A check in the amount of the fee(s) is enclosed.

Publication Fee

Payment by credit card. Form PTO-2038 is attached.

Advance Order - # of Copies _____

The Commissioner is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

Commissioner for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature)	(Date)
------------------------	--------

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant, a registered attorney or agent, or the assignee or other party to interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Washington, DC 20231.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

TRANSMIT THIS FORM WITH FEE(S)



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Adm. Comptroller of Patents and Trademarks
Washington, D.C. 20540
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,384	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-01OCIP	6340
21316	7590	04/22/2003	EXAMINER	
			KETTER, JAMES S	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 04/23/2003				

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The patent term adjustment to date is 0 days. If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the term adjustment will be 0 days.

If a continued prosecution application (CPA) was filed in the above-identified application, the filing date that determines patent term adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system. (<http://pair.uspto.gov>)

Any questions regarding the patent term extension or adjustment determination should be directed to the Office of Patent Legal Administration at (703)305-1383.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
www.uspto.gov
Washington, D.C. 20591
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/122,314	07/24/1998	STEPHEN J. ELLEDGE	BAY1364-010CIP	4340
31516	7594	04/22/2003		EXAMINER
VINSON & ELKINS, L.L.P. 100 E FANNIN STREET 2300 FIRST CITY TOWER HOLSTON, TX 77002-6760 UNITED STATES			KETTER, JAMES S	
			ART UNIT	PAPER NUMBER
			1636	
DATE MAILED: 04/22/2003				

Notice of Fee Increase on January 1, 2003

If a reply to a "Notice of Allowance and Fee(s) Due" is filed in the Office on or after January 1, 2003, then the amount due will be higher than that set forth in the "Notice of Allowance and Fee(s) Due" since there will be an increase in fees effective on January 1, 2003. See Revision of Patent and Trademark Fees for Fiscal Year 2003; Final Rule, 67 Fed. Reg. 70847, 70849 (November 27, 2002).

The current fee schedule is accessible from: <http://www.uspto.gov/main/howfees.htm>.

If the issue fee paid is the amount shown on the "Notice of Allowance and Fee(s) Due," but not the correct amount in view of the fee increase, a "Notice to Pay Balance of Issue Fee" will be mailed to applicant. In order to avoid processing delays associated with mailing of a "Notice to Pay Balance of Issue Fee," if the response to the Notice of Allowance and Fee(s) due form is to be filed on or after January 1, 2003 (or mailed with a certificate of mailing on or after January 1, 2003), the issue fee paid should be the fee that is required at the time the fee is paid. If the issue fee was previously paid, and the response to the "Notice of Allowance and Fee(s) Due" includes a request to apply a previously-paid issue fee to the issue fee now due, then the difference between the issue fee amount at the time the response is filed and the previously paid issue fee should be paid. See Manual of Patent Examining Procedure, Section 1308.01 (Eighth Edition, August 2001).

Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

Vinson & Elkins
ATTORNEYS AT LAW

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Timothy S. Corder
Direct Dial 512-542-8446
Direct Fax 512-236-3377
tcorder@velaw.com

October 3, 2002

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002
Date


Timothy S. Corder

Assistant Commissioner for Patents
Washington, D.C. 20231

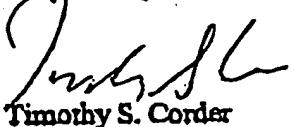
Re: U.S. Patent Application SN 09/122,384 "Rapid Subcloning Using Site-Specific Recombination," by Elledge et al.
Attorney Docket No.: BAY136/4-010CIP/36000; Client Ref.: OTA # 97-27
Confirmation No. 4340

Sir:

Enclosed for filing in the above-referenced patent application is a Preliminary Amendment for filing in the above-referenced patent application.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to appropriately deduct or credit the requisite amount from Vinson & Elkins L.L.P. deposit account No. 22-0365/BAY136/4-010CIP/36000.

Respectfully submitted,


Timothy S. Corder
Reg. No. 38,414

9282:5588

Enclosure

311729_1.DOC

AUSTIN • BEIJING • DALLAS • HOUSTON • LONDON • MOSCOW • NEW YORK • SINGAPORE • WASHINGTON, D.C.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Stephen J. Elledge et al.

Serial No.: 09/122,384

Filed: July 24, 1998

For: Rapid Subcloning Using Site-Specific Recombination

Group Art Unit: 1636

Examiner: J. Ketter

Atty. Dkt. No.: BAY136/4-10CIP/36000

Confirmation No. 4340

CERTIFICATE OF FACSIMILE

I certify that this correspondence is being transmitted on October 3, 2002, by facsimile to the Patent and Trademark Office in accordance with 37 C.F.R. §1.8.

October 3, 2002


Timothy S. Conner

PRELIMINARY AMENDMENT

VIA FACSIMILE NO. 703-746-5155

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, the Examiner is requested to please amend the above-captioned application as follows:

AMENDMENT

A. In the Claims:

Please cancel all pending claims, i.e. claims 1-20, 26, 30-35, and 37-42, and enter the following new claims:

43. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide.

44. The composition of claim 43, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.
45. The composition of claim 43, wherein the composition comprises an enzyme activity with a Cre recombinase efficiency of about 16.8% per microgram of protein.
46. An isolated nucleic acid molecule comprising a coding region wherein the coding region encodes a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
47. The nucleic acid molecule of claim 46, wherein the coding region comprises the nucleic acid sequence of SEQ ID NO:10.
48. The nucleic acid molecule of claim 46, wherein the isolated nucleic acid molecule is an expression vector.
49. The nucleic acid molecule of claim 46, wherein the coding region is operatively linked to a promoter effective to direct expression of a glutathione-S-transferase-Cre recombinase fusion polypeptide.
50. The nucleic acid molecule of claim 49, wherein the promoter is an inducible promoter.
51. The nucleic acid of claim 50, wherein the promoter is the lac promoter.
52. A host cell comprising the nucleic acid molecule of claim 46.
53. A host cell comprising the nucleic acid molecule of claim 49.
54. The host cell of claim 53, wherein the host cell expresses a Cre recombinase activity.

55. The host cell of claim 53, further defined as an *E. coli* cell.
56. A bacterial cell engineered to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
57. The bacterial cell of claim 56, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.
58. A method of producing a glutathione-S-transferase-Cre-recombinase fusion polypeptide comprising:
obtaining an expression vector comprising a coding region encoding a glutathione-S-transferase-Cre-recombinase fusion polypeptide operatively linked to a promoter;
transforming or transfecting the vector into a cell; and
growing the cell under conditions effective to express a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
59. The method of claim 58, further comprising isolating the glutathione-S-transferase-Cre-recombinase fusion polypeptide.
60. The method of claim 59, wherein isolating the polypeptide comprises glutathione affinity chromatography.
61. A method of recombining nucleic acid segments, wherein each segment comprises a *lox* site specific recombinase site, the method comprising contacting the nucleic acid segments with a glutathione-S-transferase-Cre-recombinase fusion polypeptide.
62. The method of claim 61, wherein the polypeptide has an amino acid sequence according to SEQ ID NO:11.

63. A composition comprising a glutathione-S-transferase-Cre-recombinase fusion polypeptide and one or more nucleic acid molecules, wherein the nucleic acids comprise a site specific recombinase site.
64. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a lox recombination site upstream in a 5' to 3' orientation from an amino acid encoding region.
65. The composition of claim 63, wherein at least one of said nucleic acid molecules comprises a transcription regulatory element upstream in a 5' to 3' orientation of a lox recombinase site.
66. The composition of claim 64 wherein the lox recombinase site is a *loxP*, *loxP2*, *loxP3*, *loxP23*, *loxP511*, *loxB*, *loxC2*, *loxL*, *loxR*, *lox486*, *lox4117*, or *loxH* site.
67. The composition of claim 65 wherein the lox recombinase site is a *loxP*, *loxP2*, *loxP3*, *loxP23*, *loxP511*, *loxB*, *loxC2*, *loxL*, *loxR*, *lox486*, *lox4117*, or *loxH* site.
68. The composition of claim 64, wherein the amino acid encoding region is a member of a nucleic acid library.

II. REMARKS

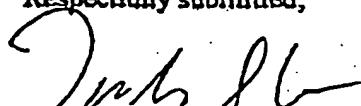
The claims in this preliminary amendment do not add new matter to the application and their entry is therefore respectfully requested. Support for the claims may be found throughout the Specification and at least in Example 3 found on page 47.

IV. CONCLUSION

Applicants respectfully submit that the present application and all claims are in condition for immediate allowance and early notice to such effect is earnestly solicited. If, in the opinion of the Examiner, a phone call may help expedite prosecution of this application, the Examiner is invited to contact the undersigned representative at (512) 542-8446.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Vinson & Elkins L.L.P. Deposit Account No. 22-0365/RAY136/4-10CIP/36000.

Respectfully submitted,



Timothy S. Corder
Reg. No. 38,414
Agent for Applicant

Vinson & Elkins L.L.P.
2300 First City Tower
1001 Fannin
Houston, Texas 77002-6760
512/542-8446

Date: October 3, 2002

CAUSE NO. 2001-61352

P-18
STIPX
PPDSXBaylor College of Medicine and
BCM Technologies, Inc.,

Plaintiffs/COUNTERCLAIM DEFENDANTS,

v.

ClonTech Laboratories, Inc.,

Defendant/COUNTERCLAIM PLAINTIFF,

Invitrogen Corporation,

ADDITIONAL COUNTERCLAIM DEFENDANT,

IN THE DISTRICT COURT

HARRIS COUNTY, TEXAS

133RD JUDICIAL DISTRICTF. CHARLES BACARISSE, D
District Clerk

OCT 29 2002

By *[Signature]* Harris County, Texas
DeputySTIPULATED PROTECTIVE ORDER

Whereas pretrial discovery in this action will necessarily involve the disclosure of trade secrets or confidential research, development, or commercial information of both parties and of non-parties from whom discovery may be sought; and

Whereas the parties have in good faith conferred and have agreed upon the terms of a Protective Order and for good cause shown; therefore

The parties stipulate, pursuant to Texas Rule of Civil Procedure 192.6, subject to the approval of the Court, to the following Protective Order:

1. Scope of Protection.

1.1 This Protective Order shall govern any record of information, designated pursuant to ¶ 2 of this Protective Order, produced in this action, including all designated deposition testimony, all designated testimony taken at a hearing or other proceeding, interrogatory answers, documents and

FAX FAXES E-MAILS AND
Tape recordings, of poor quality
and less satisfactory for photographic
recording; and/or others who were
present at the time of imaging